

PEOPLE COME FIRST AT FERRING



STandardized **RE**porting using **ADaM** **STREAM**

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Agenda

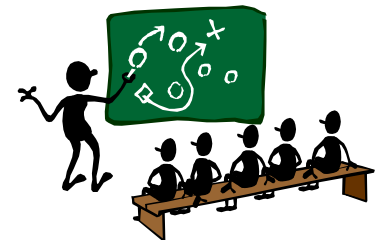
- Objective and background
- Concept
- Implementation
- Conclusion



Objective

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- Standardize and automatize the reporting of clinical data for regulatory documents
 - CTR, ISS/ISE, IB, DSUR etc.
- Minimize risk
 - manual work, copy/paste, validation
- Reduce cost and time
 - workload, resources
- Optimize resourcing
 - focus on science



Previously

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- Reporting was performed based on definition in SAP, TLF specs
- For 300-400 TLFs - developed and customised standard programs
- Any change in TLF required change in:
 - SAP
 - TLF specs
 - TLF program
 - ADaM specs
 - ADaM program
- Inefficient and caused problems with consistency



Current ADaM

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ADaM Model is now mature and stable

3 types of datasets:

- Subject level (ADSL)
- Occurrence (ADAE, ADMH, ADCM)
- **BDS (ADEF, ADLB, ADEG, ADVS)**

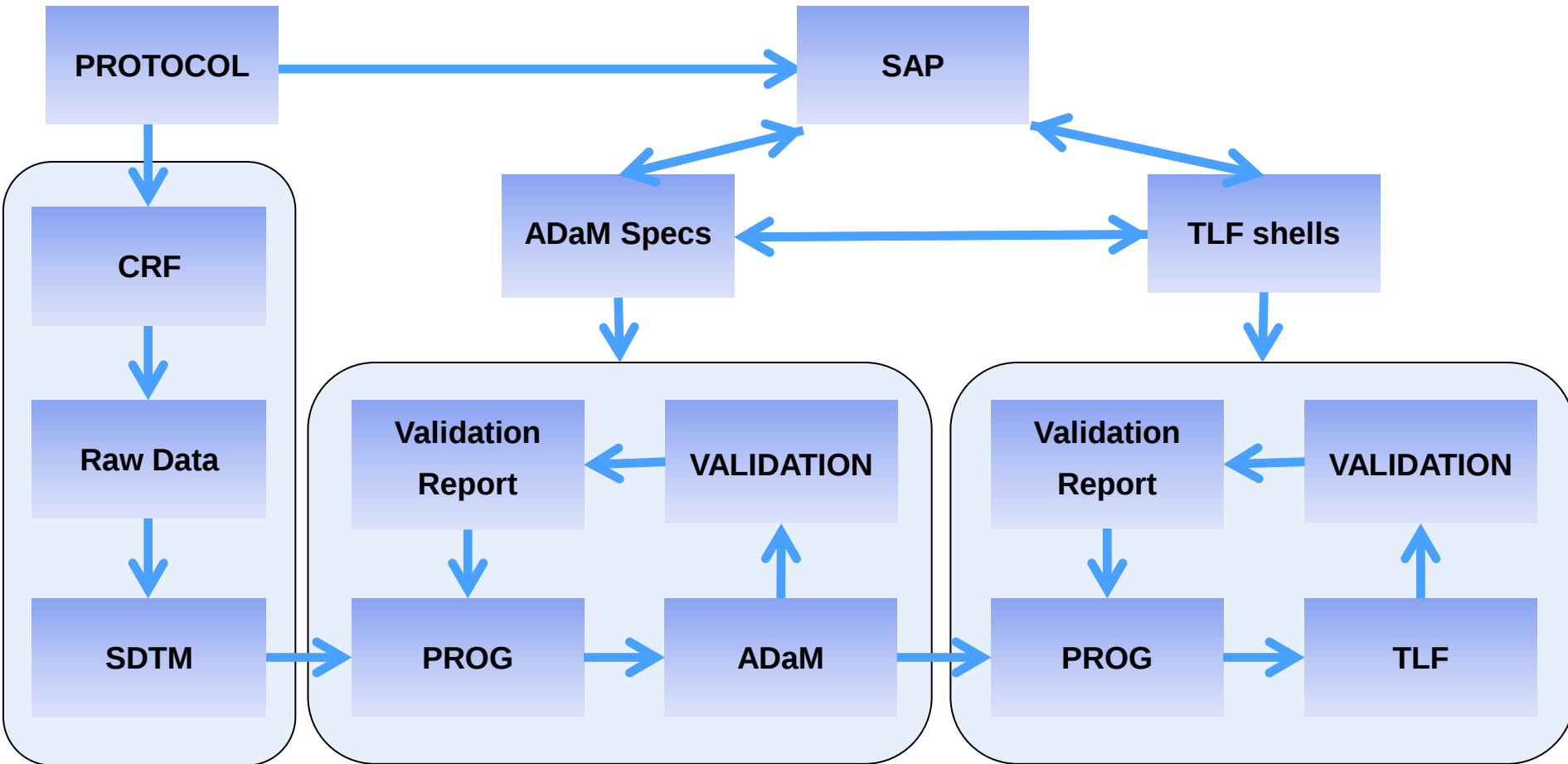


Data structure is the same but with different content

Perfectly suited for standardization of output!

Expect 99% of summary tables to be produced by 6 standard macros!

Process



Concept: ADaM BDS structure

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format	Codelist/ Controlled Terms	Source/Derivation
ADXX	PARCAT1	Parameter Category 1	Char	\$200		* See below
ADXX	PARCAT1N	Parameter Category 1 (N)	Num			* See below
ADXX	PARAM	Parameter	Char	\$200		* See below
ADXX	PARAMCD	Parameter Code	Char	\$8		* See below
ADXX	PARAMN	Parameter (N)	Num			* See below
ADXX	AVALC	Analysis Value (C)	Char	\$200		* See below
ADXX	AVAL	Analysis Value	Num			* See below

Basic BDS rule:

One-to-one mapping rule:

- PARAMCD - PARAM - PARAMN
- AVALC – AVAL (within PARAM)
- Categorical: AVALC sorted by AVAL

Tables - 1

Embryo Evaluation Subject Level: Insemination - Intention-To-Treat Analysis Set

	Treatme 1		Treatme 2		Total	
Insemination						
Method of insemination, N (%)						
IVF	10	(10.5%)	12	(11.8%)	22	(11.2%)
ICSI	75	(78.9%)	74	(72.5%)	149	(75.6%)
Total	95	(100%)	102	(100%)	197	(100%)
MII oocytes						
N	75		74		149	
Mean	7.81		6.59		7.21	
SD	4.42		4.13		4.31	
Median	7		6		6	
p25	4		4		4	
p75	10		8		9	
min	1		1		1	
max	24		24		24	

N: Number of observations, %: Percentage of observations

Tables - 2

Transvaginal Ultrasound: Endometrium - Intention-To-Treat Analysis Set

	Treatme 1		Treatme 2		Total	
Stimulation day 6 (cos 1)						
Endometrial triple-layer structure, N (%)						
Yes	59	(95.2%)	68	(94.4%)	127	(94.8%)
No	3	(4.8%)	4	(5.6%)	7	(5.2%)
Total	62	(100%)	72	(100%)	134	(100%)
Endometrial thickness (mm)						
N	62		72		134	
Mean	7.73		7.81		7.77	
SD	1.68		1.82		1.75	
Median	7.45		7.65		7.5	
p25	6.5		6.5		6.5	
p75	8.5		9.1		9	
min	4.47		4		4	
max	12.3		13		13	

N: Number of observations, %: Percentage of observations

Tables – Metadata linked to ADaM

Transvaginal Ultrasound: Endometrium Intention-To-Treat Analysis Set

Treatme 1 Treatme 2 Total

FORMATS

Stimulation day 6 (cos 1)

Endometrial triple-layer structure N (%)

Yes	59	(95.2%)	68	(94.4%)	127	(94.8%)
No	3	(4.8%)	4	(5.6%)	7	(5.2%)
Total	62	(100%)				

Endometrial thickness (mm)

N	62
Mean	7.73
SD	1.68
Median	7.45
p25	6.5
p75	8.5
min	4.47
max	12.0

N: Number of observations, %: Percentage of observations

Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1	Parameter Category 1
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARAM	Parameter
ADXX	PARAMCD	Parameter Code
ADXX	PARAMN	Parameter (N)
ADXX	AVALC	Analysis Value (C)
ADXX	AVAL	Analysis Value

Generic Tables



<PARCAT1 by PARCAT1N> - <ANALYSIS SET FORMAT>

<ACTARM 1>

<ACTARM 2>

Total

<GROUP by GROUPN (e.g. AVISIT by AVISITN)>

<PARAM by PARAMN>

If PARAM is categorical then present as

<PARAM>, n (%)

<AVALC by AVAL> xxx (xx%)

Total xxx (100%)

If PARAM is continuous then present as

<PARAM>

n xxx

Mean (SD) xx.x (xx.x)

Median xx.x

IQ-range xxx; xxx

Range xxx; xxx

n: Number of observations

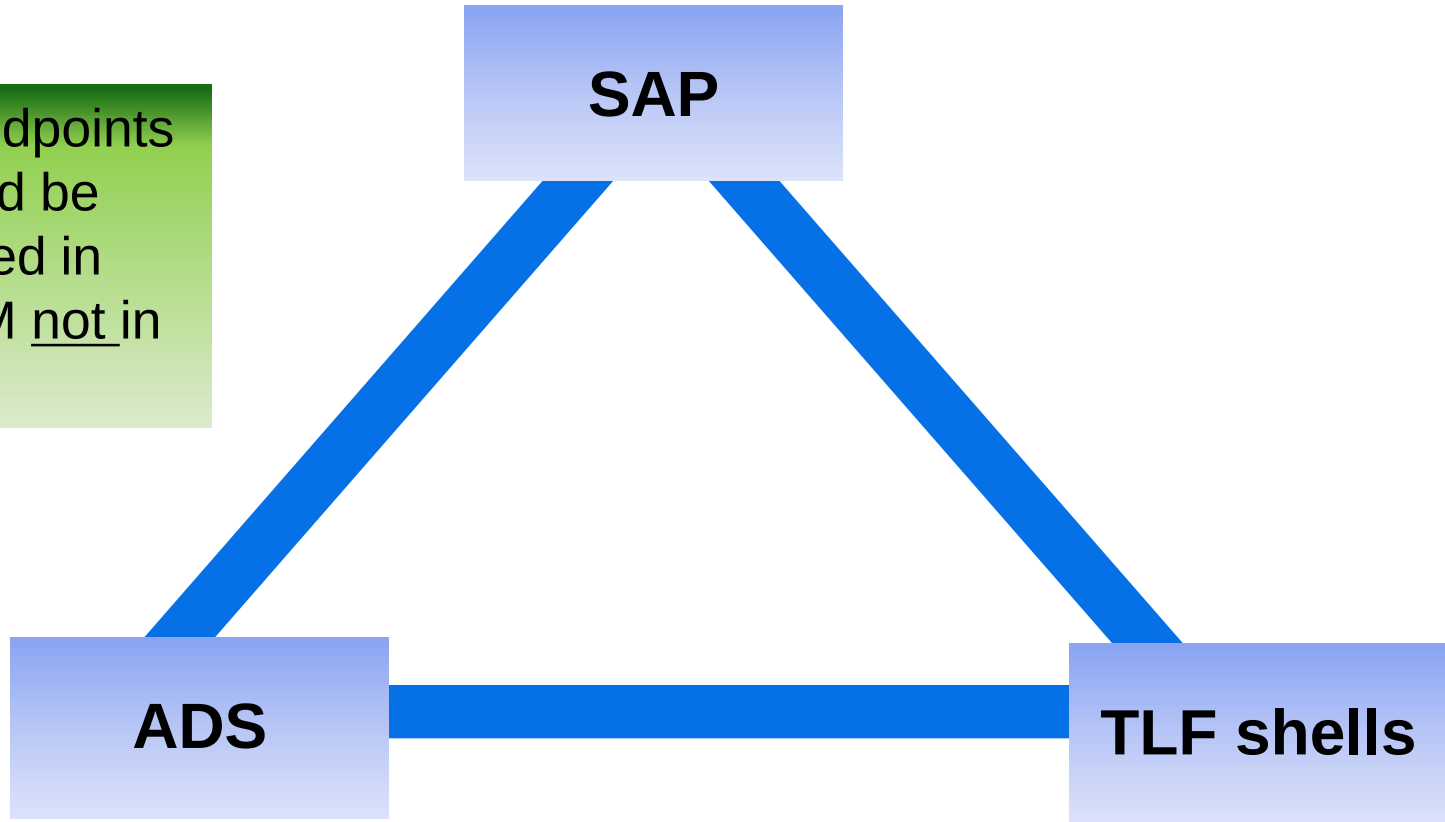
?: Percentage of observations

FE999049/ART/000004/DDMMYYYY-XXX/PROGNAME.SAS

Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1	Parameter Category 1
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARAM	Parameter
ADXX	PARAMCD	Parameter Code
ADXX	PARAMN	Parameter (N)
ADXX	AVALC	Analysis Value (C)
ADXX	AVAL	Analysis Value

Implementation

All endpoints
should be
created in
ADaM not in
TLFs



7.1 Demographics and Other Baseline Characteristics

All relevant baseline data will be tabulated including both treatment groups and a total column. Tabulations will be produced overall and by age-strata for both the mITT and the PP analysis set.

[...]

7.1.4 Infertility History

The following data on infertility history obtained at the screening visit will be tabulated: Number of subjects with primary infertility, duration of infertility (months), and primary reason for infertility.

7.1.5 Previous Fertility Treatment Cycles

The following data on previous fertility treatment cycles obtained at the screening visit will be tabulated: Number of subjects with at least one previous fertility treatment cycle, number of previous fertility treatment cycles per subject, number of subjects with at least one clinical pregnancy, number of clinical pregnancies per subject, number of subjects with at least one live birth, and number of live births per subject.

7.1.6 Menstrual History

The average duration of the menstrual cycle (days) will be tabulated.

7.1.7 Reproductive History

The following data on reproductive history following natural conception obtained at the screening visit will be tabulated: Number of subjects with at least one previous clinical pregnancy, number of clinical pregnancies per subject, number of subjects with at least one live birth, and number of live births per subject.

Consistency through ADaM Specs

7.1.4 Infertility History

The following data on infertility history obtained at the screening visit will be tabulated. Number of subjects with primary infertility, duration of infertility (months), and primary reason for infertility.

Infertility History - Full Analysis Set

Full Analysis Set

Primary infertility

Duration of infertility (months)

Mean (SD)

Median (P25;P75)

Min;max

Primary reason for infertility

Dataset Name	PARCAT1N	PARCAT1	PARAMN	PARAMCD	PARAM
ADXX	1	Infertility History	11	PRIMINF	Primary infertility
			12	INFDUR	Duration of infertility (months)
			13	PREASON	Primary reason for infertility

Consistency through ADaM Specs

Infertility History - Full Analysis Set

	Treatment1		Treatment2		Total	
	N	(%)	N	(%)	N	(%)
Full Analysis Set	xx	(100%)	xx	(100%)	xx	(100%)

Primary infertility*

Yes

No

Total

Duration of infertility (months)

N

Mean (SD)

Median (P25;P75)

Min;max

Primary reason for infertility

Unexplained infertility

Tubal infertility

Mild male factor

Moderate male factor

Severe male factor

Anovulatory, WHO Group I

Anovulatory, WHO Group II

Endometriosis stage I/II

Endometriosis stage III/IV

Other

Total

Dataset Name	PARCAT1N	PARCAT1	PARAMN	PARAMCD	PARAM	AVAL	AVALC
ADAX	1	Infertility History	11	PRIMINF	Primary infertility	1 2	Yes No
			12	INFDUR	Duration of infertility (months)	Numeric	
			13	PREASON	Primary reason for infertility	1 2 3 4 5 6 7 8 9 10	Unexplained infertility, Tubal infertility, Mild male factor, Moderate male factor, Severe male factor, Anovulatory, WHO Group I, Anovulatory, WHO Group II, Endometriosis stage I/II, Endometriosis stage III/IV, Other

N = Number of subjects, % = Percentage of subjects

* Primary infertility: No previous clinical pregnancy

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PHARMACEUTICALS

[illegible]

Tables

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Table layouts are based on:

2 types of datasets:

- Occurrence (ADAE, ADMH, ADCM)
- BDS (ADEF, ADLB, ADEG, ADVS)
- 6 Generic table layouts



Tables – Common Mockups



Template - 1

Overall summary of treatment emergent adverse events - <safety population text>

	Treat 1 (N=xxx)			Treat 2 (N=xxx)			Total (N=xxx)		
	n	(%)	E	n	(%)	E	n	(%)	E
Adverse events	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Severe adverse events	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Adverse drug reactions	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Adverse events leading to discontinuation	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Serious adverse events	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Adverse events leading to death	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx

N = Number of subjects

n = Number of subjects with observation

% = Percentage of subjects with observation

E = Number of observations

Tables – Common Mockups



Template - 2

Incidence of treatment emergent adverse events by MedDRA system organ class and preferred term - <safety population text>

MedDRA system organ class/ preferred term	Treat 1 (N=xxx)			Treat 2 (N=xxx)			Total (N=xxx)		
	n	(%)	E	n	(%)	E	n	(%)	E
Any adverse events	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Body system organ class 1	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 1	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 2	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 3	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 4	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Body system organ class 2	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 1	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 2	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 3	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Preferred term 4	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx

N = Number of subjects

n = Number of subjects with observation

% = Percentage of subjects with observation

E = Number of observations

Tables – Common Mockups



Template - 3

Concomitant medication by ATC level 1 and ATC level 2 - <population text>

ATC level 1 / ATC level 2	Treat 1 (N=xxx)			Treat 2 (N=xxx)			Total (N=xxx)		
	n	(%)	E	n	(%)	E	n	(%)	E
Any concomitant medication	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 1 <1>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <1>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <2>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <3>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <4>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 1 <2>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <1>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <2>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <3>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
ACT level 2 <4>	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx

N = Number of subjects

n = Number of subjects with observation

% = Percentage of subjects with observation

E = Number of observations

Tables – Common Mockups



Template - 4

Template for BDS change macro - <population text>

	Treat 1 (N=xxx)		Treat 2 (N=xxx)		Total (N=xxx)	
	Value	Change from baseline	Value	Change from baseline	Value	Change from baseline
Param 1						
Baseline						
n	xxx		xxx		xxx	
Mean (SD)	x.x (x.xx)		x.x (x.xx)		x.x (x.xx)	
Median (P25;P75)	x.x (x.x;x.x)		x.x (x.x;x.x)		x.x (x.x;x.x)	
Min;max	x;x		x;x		x;x	
Visit 2						
n	xxx	xxx	xxx	xxx	xxx	xxx
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median (P25;P75)	x.x (x.x;x.x)	x.x (x.x;x.x)	x.x (x.x;x.x)	x.x (x.x;x.x)	x.x (x.x;x.x)	x.x (x.x;x.x)
Min;max	x;x	x;x	x;x	x;x	x;x	x;x

N = Number of subjects

Tables – Common Mockups

Template - 5

Template for BDS macro - <population text>

	Treat 1 (N=xxx)			Treat 2 (N=xxx)			Total (N=xxx)		
	n	(%)	E	n	(%)	E	n	(%)	E
Param 1									
Category 1	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Category 2	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Category 3	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx
Category 4	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx	xxx	(xx.x)	xxx

N = Number of subjects

n = Number of subjects with observation

% = Percentage of subjects with observation

E = Number of observations

Tables – Common Mockups

Template - 6

Template for BDS macro - <population text>

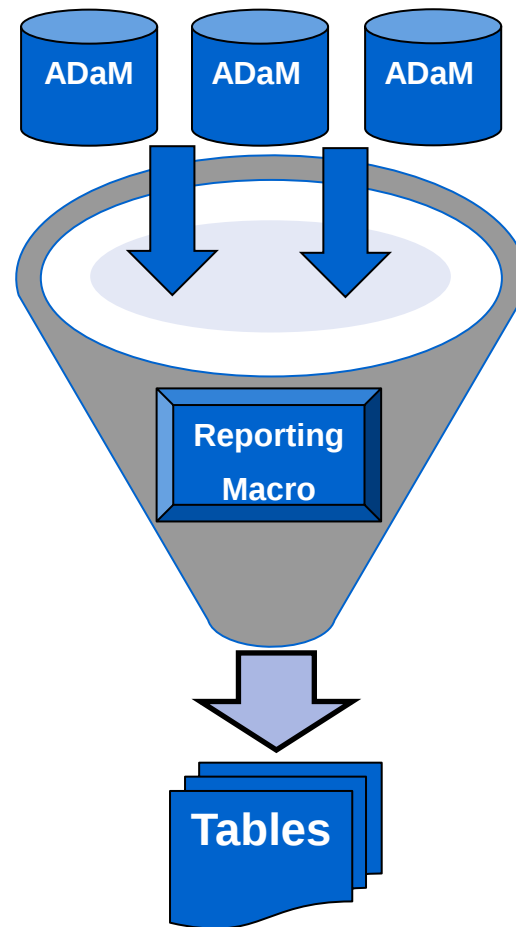
	Treat 1 (N=xxx)	Treat 2 (N=xxx)	Total (N=xxx)
Param 1			
n	xxx	xxx	xxx
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median (P25;P75)	x.x (x.x;x.x)	x.x (x.x;x.x)	x.x (x.x;x.x)
Min;max	x;x	x;x	x;x
Param 2, n (%)			
Category 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Category 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Category 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
Category 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
All	xxx (100.0)	xxx (100.0)	xxx (100.0)

N = Number of subjects

n = Number of subjects with observation

% = Percentage of subjects with observation

Standard Reporting Macros



Summary statistics on BDS data

Infertility history: All subjects - Modified Intention-To-Treat Analysis Set

Menstrual history: All subjects - Modified Intention-To-Treat Analysis Set

Previous fertility treatment cycles: All subjects - Modified Intention-To-Treat Analysis Set

	Average	Treatment1 (N=xxx)	Treatment2 (N=xxx)	Total (N=xxxx)
Primary infertility				
No				
Yes				
All				
Duration (n)				
Mean (n)				
Median				
Min;max				
Previous stimulation				
No				
Yes				
All				

PARCAT1N = 2)),

%t_bds_sumcat[inds = ADAM.ADHIS(where = (PARCAT1N = 3)),
sl_inds = ADAM.ADSL2,
outlib = EFFICACY,
pop = MITTFL,
address = ADAM.2.1ALL

Loop over PARCAT1 in ADaM

Other	8	3 (<x%)	4 (<x%)	7 (<x%)
All	9	4 (<x%)	6 (x%)	10 (x%)
	10	3 (<x%)	1 (<x%)	4 (<x%)
	11	1 (<x%)		1 (<x%)
	12	2 (<x%)	1 (<x%)	3 (<x%)
	16	1 (<x%)		1 (<x%)
	All	xxx (100%)	xxx (100%)	xxx (100%)
Previous clinical pregnancy, n (%)				
No	xxx (xx%)	xxx (xx%)	xxx (xx%)	
Yes	xx (x%)	xx (x%)	xx (x%)	
All	xxx (100%)	xxx (100%)	xxx (100%)	

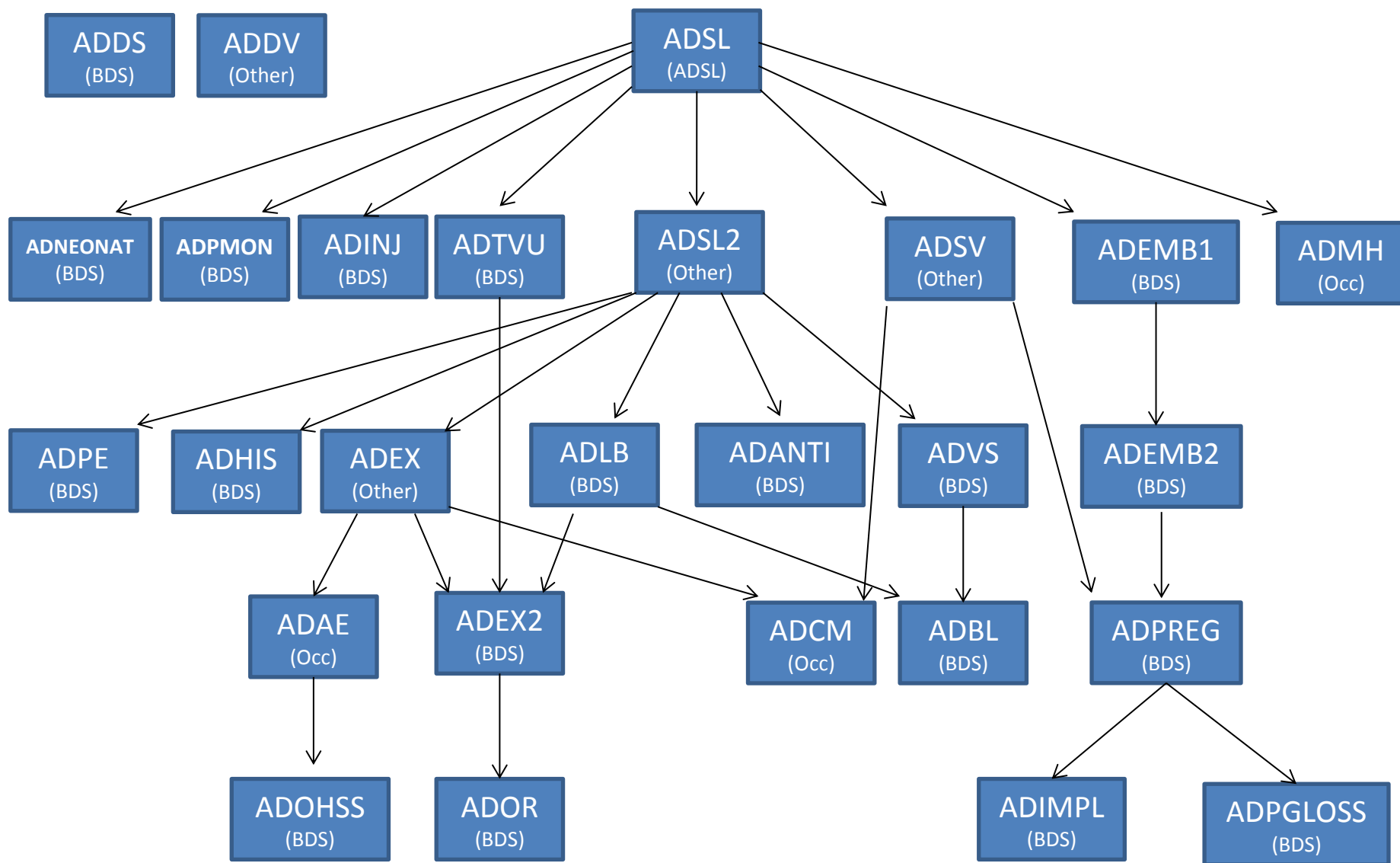
N = Number
n = Number
% = Percent

N = Num

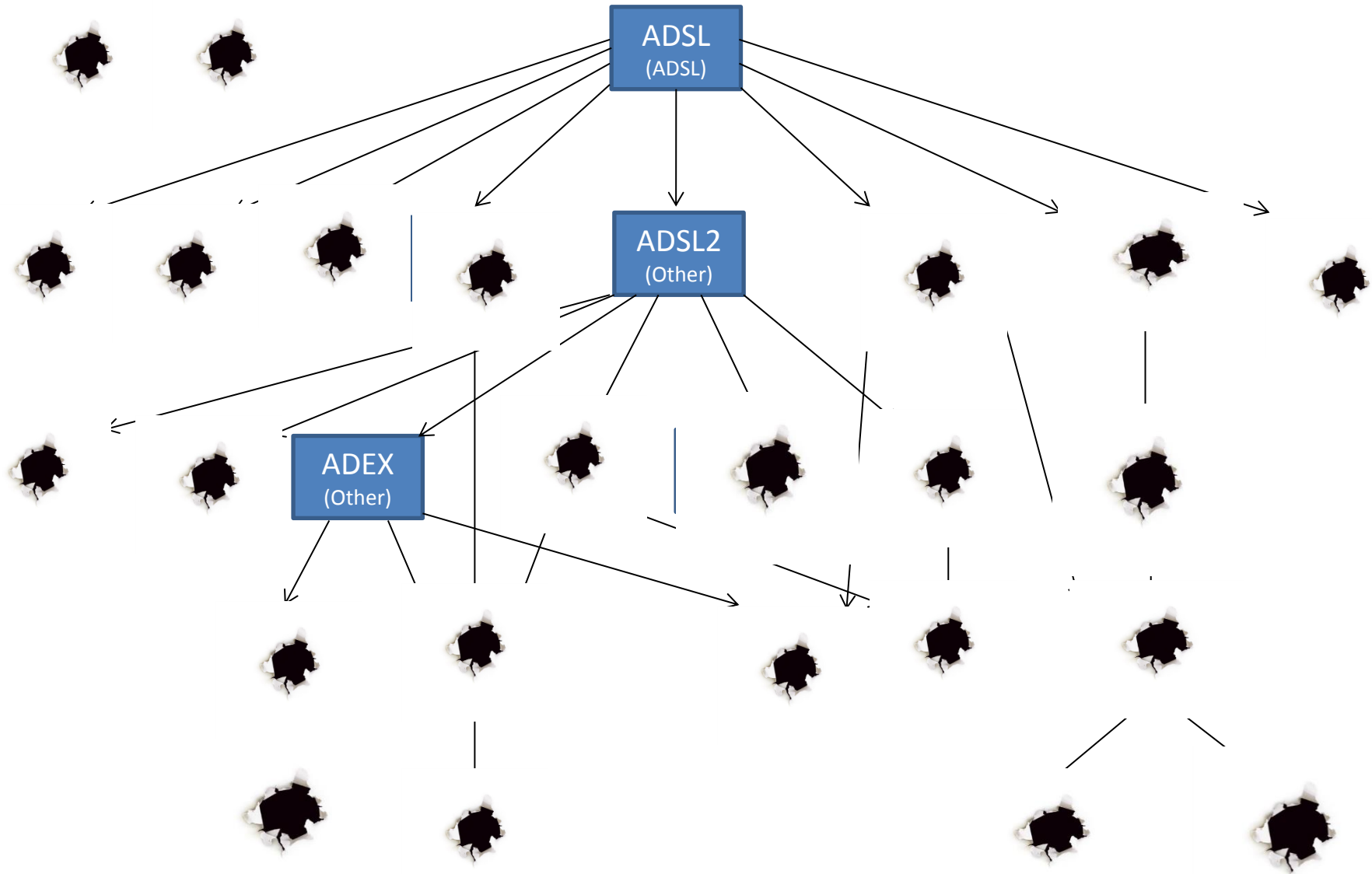
N = Number of subjects
n = Number of subjects with observation
% = Percentage of subjects with observation



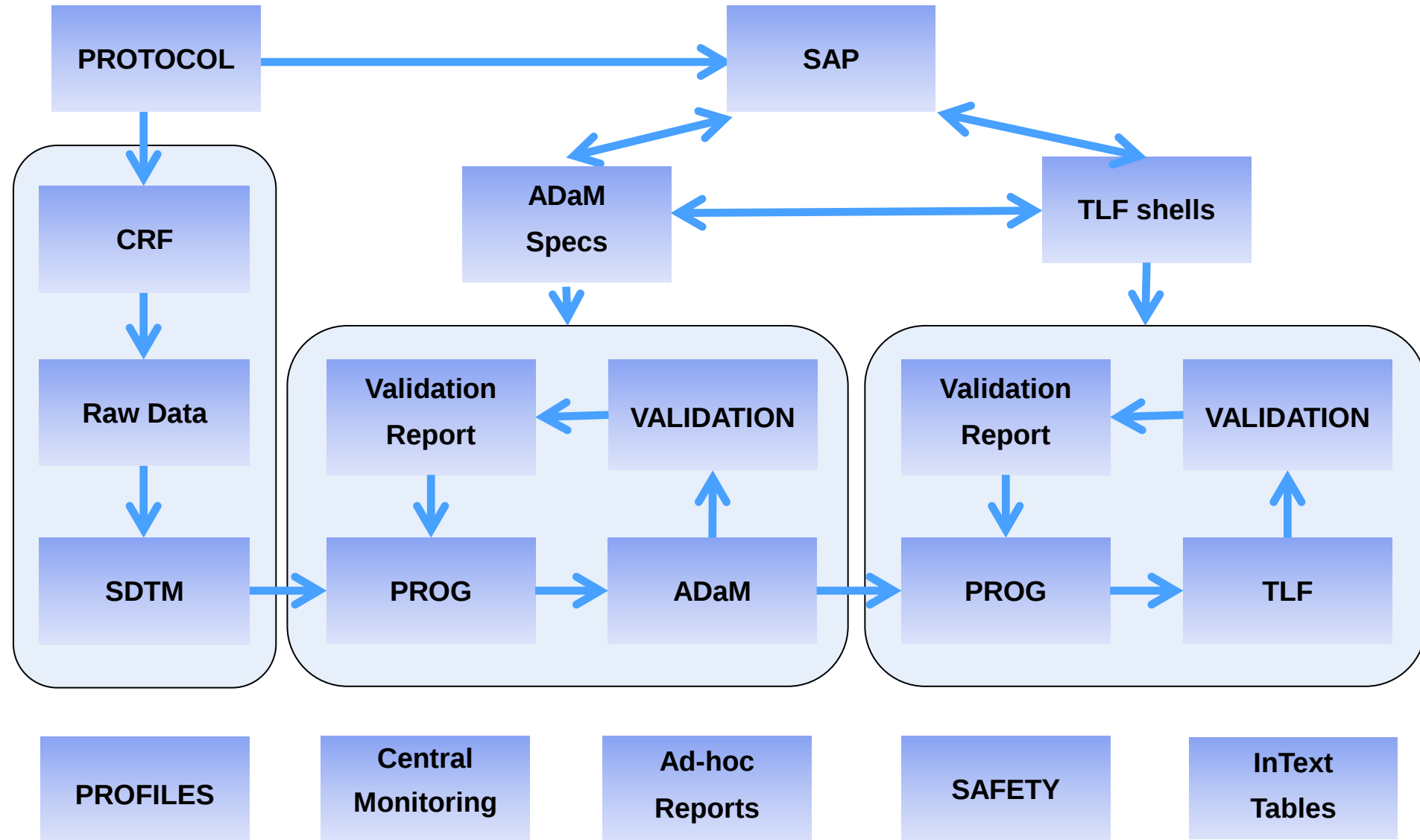
Standard Macro / Summary Tables (Example)



Standard Macro / Summary Tables (Example)



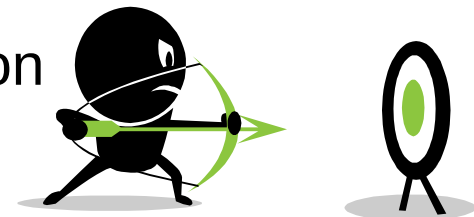
STREAM – Process & Consistency



Conclusion

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- Design SAP while keeping STREAM in mind
- Put more effort in designing ADaM (with all metadata for TLF generation)
- Generic TLF specs
- Use standard macros for the majority of the summary tables
- Generate more TLFs using less effort
- Ensures consistency across all deliverables
- Less effort for TLF programming and validation



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STandardized **RE**porting using **ADaM** **STREAM**

Thank you!